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CLINICAL MEDICINE

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AUTHORITATIVE UNDERSTANDABLE PRACTICAL

APRIL 1948

Vol. 55 No. 4

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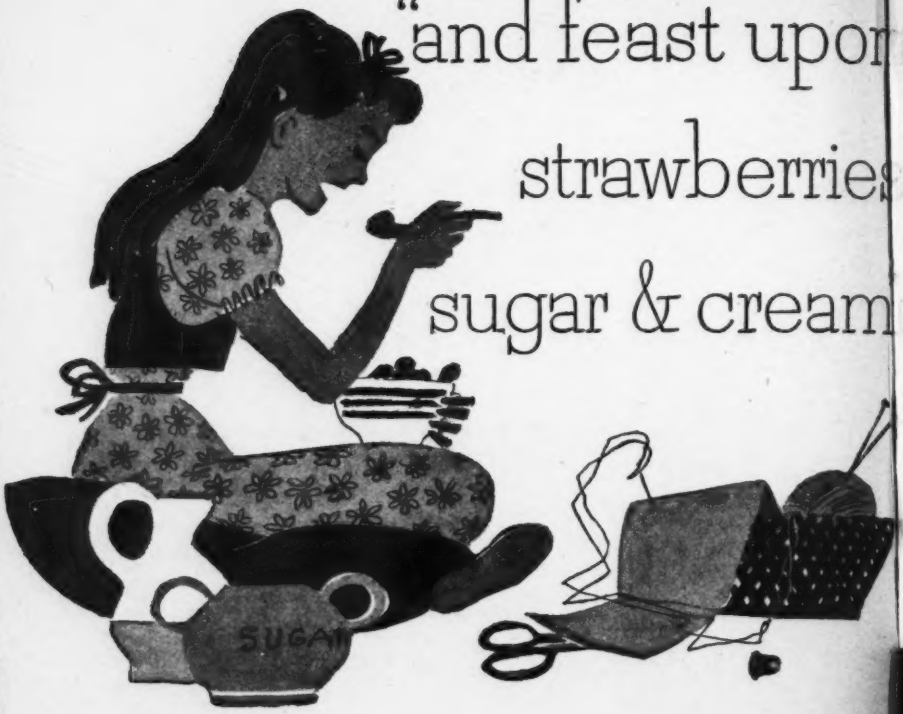

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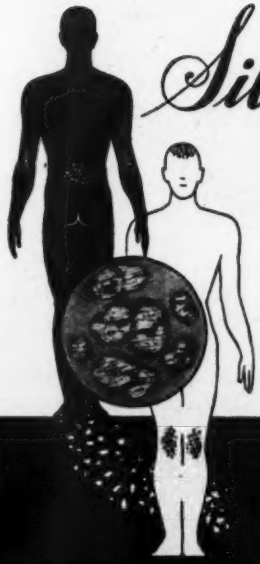

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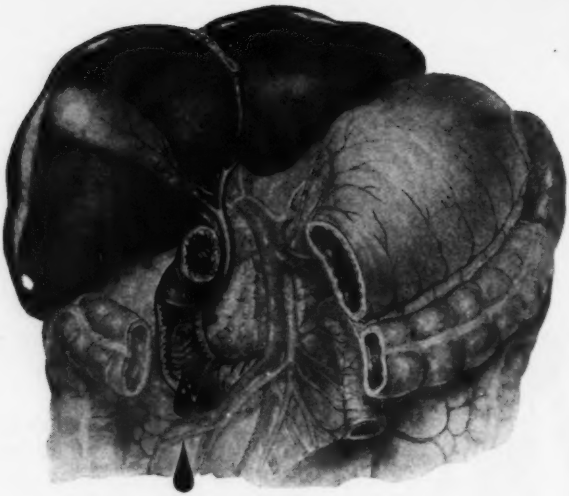

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CLINICAL MEDICINE

APRIL, 1948

Volume 55, No. 4

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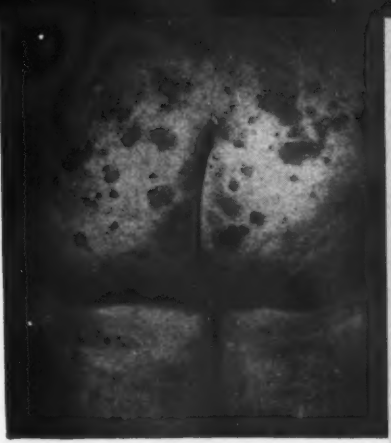

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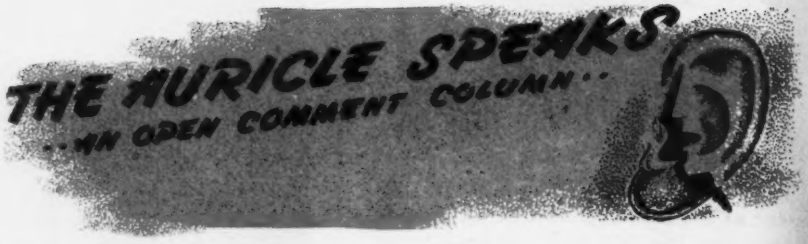

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"Because it's a check," Dr. Medico assured him.

"Well, if that's a check it's certainly in a new dress," the teller averred.

"Isn't it dated?" Dr. Medico demanded.

"It certainly is."

"And directed to your bank?"

"Certainly is."

"And directed you to pay a certain sum of money?"

"Yes—that's true."

"Well, then, why isn't it a check, when it's signed by the debtor?"

"It's certainly a new one on me, but I'll pay it, and take a chance," the teller agreed, and the Supreme Court of Arkansas upheld him in a case reported in 229 S. W. 1026, where the Court ruled that such a document fulfilled all the requirements of an actual check.

"The telegraphic message from the debtor patient can be treated as the equivalent of a written check or order for the payment of the money," was the reasoning of the Court.—Judge M.L.H.

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There are now over 700 medical groups practicing in the United States. During the period 1940 to 1946, between 1/5 and 1/3 of the groups which were active in 1940 have disbanded or ceased to operate as groups, during the 6 year period.

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There is a tendency toward increased

(Continued on page 10)

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1. Gusberg, S. B., Am. Jl. Obst. & Gyn. 50:502, 1945.

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THE AURICLE SPEAKS

(*Continued from page 8*)

size of the groups during the past 6 years. The great majority of the physicians are employed full time. Smaller groups are usually found in the smaller cities, and larger groups in the larger cities, but 33% of the large groups (that is, those with 11 or more full time physicians) are located in communities of less than 25,000 population.

Practically all groups furnish surgery and medicine, with a diminishing number furnishing obstetrics, x-ray, gynecology, pediatrics, eye-ear-nose-and-throat and least of all, dentistry.—G. H. HUNT and M. S. GOLSTEIN in *J.A.M.A.*, Dec. 6, 1947.

It has been well said that instead of trying to make ourselves happier and other people better, we should make ourselves better and othe people happier.

Euthanasia

We all know cases that would benefit if euthanasia were legalized. Perhaps we are swayed by our own instinctive desires to live, by acquired medical teachings to stubbornly wage war against disease by all means and to the last gasp.

The question is "Why should doctors be leaders in the movement for euthanasia?" The answer is obviously "Because we are so close to the entire matter." However, the layman as a whole should be concerned.

Why should we medical men take it upon ourselves to actually prepare this "dirty job," even though it is a noble job. Are we not associated enough with sickness and death as it is? Do we not already symbolize illness in the minds of so many people already? Are we not indeed identified with tormenting pain?

The public, or a part of us, think of us in terms of saviours and helpers, then why spoil the role?

Then, comes the question as to whether we are to be regarded as morally liable. The sins and mistakes of a minority might smirch the entire medical fellowship.—B. LIBER, M.D. (New York City) in *Medical Records*, Oct. 1947

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The Plasma Protein Fractions and Their Therapeutic Uses

By CHARLES D. MARPLE, M.D., *New York City*

From the Department of Medicine (Vascular Disease Research Laboratory) of the New York Hospital—Cornell University Medical School, New York City.

THE blood is a complex fluid in which solid elements, the blood cells, are suspended. This constitution is indicated in Table I.

TABLE I. THE COMPOSITION OF THE BLOOD

I. SOLID ELEMENTS (approx. 45 percent of blood volume).
- A. Erythrocytes (Red blood cells).
- B. Leukocytes (White blood cells).
- C. Thrombocytes (Platelets).

II. FLUID PORTION or PLASMA* (approx. 55 percent of blood volume).
- A. Water (91-92 percent of plasma volume).
- B. Solids (8-9 percent of plasma volume).
  1. Inorganic Constituents (0.9 percent of plasma volume). Sodium, calcium, potassium, magnesium as chlorides, sulfates, bicarbonates and phosphates; iron, copper.
  2. Plasma Proteins (6-8 percent of plasma volume). Albumins, globulins and fibrinogen.
  3. Complex organic substances elaborated by the body for specific biological functions. Some of these are simple proteins, others are compound proteins (contain a non-protein prosthetic group in addition to a protein component), while those for which no protein component has been identified are undoubtedly linked to proteins in the circulating plasma.
     - a. Hormones.
       - i. Hormones known to be proteins: anterior pituitary hormones, parathyroid hormone, insulin, renal hormones.
       - ii. 17-ketosteroids: adrenal cortical hormones, male and female sex hormones (estrogens, corpus luteum hormones, androgens).
       - iii. Others, including adrenalin, and those as yet poorly understood, e.g., sympathin, and so on.
     - b. Enzymes. Some enzymes are simple proteins, others compound proteins. Apparently all contain protein components.
     - c. Antibodies. Apparently all antibodies contain, or are attached to proteins in the circulating plasma and the major portion are found in the gamma globulin fraction of the plasma.
  4. Organic Constituents Other Than Proteins.
     - a. Non-protein nitrogenous substances. Include urea and uric acid, xanthines and hypoxanthines, creatine and creatinine, amino-acids.
     - b. Lipids. Include cholesterol, the phospholipids, neutral fats and fatty acids.
     - c. Carbohydrates, including glucose and lactic acid.
     - d. Serum pigments including bilirubin and adsorbed pigments (carotene).

*Serum is that clear fluid which is expressed from the blood clot as the latter contracts. Serum differs from plasma in the loss of fibrinogen and of portions of other plasma constituents, utilized in or removed by the process of coagulation.

Functions of Plasma Proteins

The protein constituents of the blood plasma are discussed commonly in three general groups, albumins, globulins and fibrinogen, which are clearly defined by their chemical properties and physiological functions. Thus, the function of albumin in maintaining the osmotic pressure of the blood and of fibrinogen participating in the phenomenon of blood coagulation has long been appreciated. The principle functions of the plasma proteins are summarized in Table II.

Fractionation of Plasma

Until quite recently the plasma proteins were separated by relatively crude chemical methods—"salting out" with concentrated salt solutions, precipitation by organic solvents and precipitation at the specific iso-electric point of the protein. The development of the methods of ultracentrifugation (Svedberg), of electrophoresis (Tiselius) and of chemical fractionation (Harvard group) has permitted a more highly refined and a considerably more detailed separation of the plasma proteins. In any method, the cellular elements are first removed by the mechanical device of centrifugation. It should be remembered that the cellular elements themselves contain proteins; the erythrocytes, the respiratory pigment (hemoglobin) and a large number of protein enzymes, and the white blood cells, the enzyme verdoperoxidase and probably thromboplastic substances.

The method of Cohn and his associates for the fractionation of plasma proteins yields six major fractions (some of which have already been subfractionated) See Table III.

Plasma Globulins

The fractionation of plasma (1, 2) has thus made available the albumins for use in shock, edema nd hypoproteinemic states and the specific globulins of use in blood coagulation and for the prevention or attenuation of certain infectious diseases. Fractionation has also permitted the isolation of many of the smaller organic molecules which exist in highly specific combination with the larger proteins and whose separation as naturally occurring complexes permits study of their physiochemical interactions and physiological roles. Table IV lists specific plasma globulins so far isolated and their interactions.

Serum Albumin

Normal human serum albumin (3) was developed during the War primarily as a blood substitute for use in traumatic shock. The qualities which endowed it with particular value in this role are summarized in Table V.

The usefulness of serum albumin is extended to several fundamental clinicopathological states and to a wide field in physiological research. See Table VI.

SHOCK (4, 5, 6). Traumatic shock primarily due to the loss of whole blood (except when there is loss of plasma through burned or denuded areas of body surface, or into the peritoneal cavity because of irritation) is treated best by the replacement of whole blood to avoid the anemia which develops if plasma or albumin are used for replacement. However, either plasma or albumin are useful for emergency supportive therapy.

When concentrated albumin is administered intravenously to patients in shock, there is a much greater increase in plasma volume than can be accounted for by the volume of solution injected, indicating that the osmotic effect of the albumin draws fluid from the tissue spaces into the circulation. Quantitatively, this increase in plasma volume approaches the increase expected on the basis of osmotic pressure measurements in vitro. Circulatory dynamics are improved and there is an increase in cardiac output greater than that produced by use of whole blood. This is explained by the increase in blood volume unaccompanied by an in-

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TABLE II. THE FUNCTIONS OF THE PLASMA PROTEINS

I. MAINTENANCE OF OSMOTC PRESSURE OF THE BLOOD AND REGULATION OF FLUID BALANCE.

The capillary membranes are relatively impermeable to the plasma proteins because of the relatively large size of the protein molecules. The proteins, therefore, exert a considerable osmotic attraction for tissue fluid. Starling's concept is that the exchange of fluid between the tissue spaces and the blood stream is regulated by a balance between the opposing forces of the hydrostatic pressure in the capillaries and the partial osmotic pressure of the plasma proteins. Where the hydrostatic pressure is high, in the proximal portion of the capillaries, there is a tendency for fluid, with its dissolved electrolytes and nutritive content, to leave the vessels. Where the hydrostatic pressure is low, as in the distal portions of the capillaries, the balance is reversed and tissue fluid is drawn into the circulation. Albumin has three times the colloidal osmotic pressure of globulin.

II. DYNAMIC EQUILIBRIUM OF BODY PROTEINS.

Starling's concept is modified to the extent that the impermeability of the capillary membranes is realized to be only relative. Amino acid aggregates, derived from absorbed food proteins and transported by the blood stream may pass through the walls of the capillaries to the organs and tissues of the body for hydrolysis, resynthesis and utilization.

III. PROTEIN RESERVES OF THE BODY.

Complementary to the above concept is the view that protein stores in the tissues are in dynamic equilibrium with the plasma proteins. In this connection, the blood may be looked upon as an organ of considerable size which contains a considerable store of protein.

IV. VEHICULAR FUNCTION.

Plasma proteins act as carriers for many substances attached to them by chemical combination or by adsorption. Such substances include bilirubin, thyroxin, uric acid, cholesterol, carotene, phospholipids, calcium (non-ionized portion), iodine and other hormones and salts.

V. BLOOD COAGULATION.

Fibrinogen and plasma prothrombin are essential elements in the phenomenon of blood coagulation.

VI. MAINTENANCE OF ACID-BASE BALANCE IN THE BLOOD.

A small portion of the alkali-binding power of the blood is due to plasma proteins, but their effect is of such small magnitude that even marked hypoproteinemia impairs only slightly the buffer systems of the blood.

VII. MAINTENANCE OF BLOOD VISCOSITY.

Proteins endow the blood with a high degree of viscosity which may contribute to the maintenance of blood pressure.

VIII. IMMUNITY.

The major portion of the antibodies in adult blood plasma have been found in the gamma globulin fraction of the blood proteins.

TABLE III. PLASMA FRACTIONS AS OBTAINED BY THE DEPARTMENT OF PHYSICAL CHEMISTRY, HARVARD MEDICAL SCHOOL

FRACTION	CONTENT
FRACTION I.	Most of the fibrinogen and the antihemophilic globulin.
FRACTION II.	Gamma globulin antibodies of proven value in measles and infectious hepatitis.
FRACTION III-1.	Antibodies, including those to typhoid 0, and isoagglutinins, including the Rh antibodies.
FRACTION III-2.	Prothrombin and one of the components of complement.
FRACTION III-3.	Plasminogen (precursor of plasmin, the fibrinolytic enzyme.)
FRACTION III.-0	Lipoproteins, which, with the lipoproteins in the next fraction, bear cholesterol, carotene, and such steroids as estriol and vitamin A.
FRACTION IV-1.	Lipoproteins of a totally different chemical structure.
FRACTION IV-4.	Variety of hormones and enzymes, including hypertensinogen and thyrotropin, a serum esterase, a carbohydrate rich alpha-globulin and an iron-binding protein presumably responsible for the transportation of iron in the plasma.
FRACTION V.	Human serum albumin. (Osmotic activity far greater than that of all other fractions combined.)
FRACTION VI.	Large amount of salts and a small amount of protein.

TABLE IV. INTERACTIONS OF BLOOD PROTEINS

(From: Cohn, E.J.: Ann. Int. Med., v. 26, 3, pp. 341-52, March 1947)

PROTEIN	FRACTION	INTERACTING MOLECULE	ORIGIN OF INTERACTING MOLECULES	PHYSIOLOGICAL FUNCTION
Hemoglobin	Red Cells	Oxygen	Air	
Carbonic Anhydrase	Red Cells	Carbon Dioxide	Tissues	Respiration
Prothrombin	III-2	Thromboplastin	Tissues	
Fibrinogen	I	Thrombin	Prothrombin	Clot Formation
Gamma Globulins	II	Antigens		
Complement: C'1	III-1		Viruses and Bacteria	Immunity
C'2	III IV			
Isoagglutinins	III-1		Red Cells	
Hypertensinogen	IV-4	Renin	Kidney	
Hypertensinase	Red Cells and Plasma	Hypertensin	Hypertensinogen	Blood Vessel Constriction
Beta$_1$ Lipoprotein	III-0	Estriol, Vit. A		
Alpha$_1$ Lipoprotein	IV-1	Vitamin A		Lipid Transport
Choline Esterase	Red Cells	Choline Esters		
Serum Esterase	IV-6	Choline Esters*		Ester Hydrolysis
Phosphatase (Alkaline)	IV	Phosphoric Acid Mono Esters		
Plasminogen**	III-3	Proteins	Plasma	Protein Hydrolysis
Iron Binding Serum Globulin	IV-7	Iron		Iron Transport

*Hydrolyzes Methyl Butyrate. **Fibrinolytic Enzyme Precursor.

TABLE V. CHEMICAL PROPERTIES OF SERUM ALBUMIN AND THEIR SIGNIFICANCE

PROPERTIES	PRACTICAL IMPLICATION
Stability in concentrated solution. (Salt poor albumin in a new diluent can be heated for 10 hours at 60° C. in the final container before distribution.)	Compact to transport Convenient to use. Eliminates need for potentially injurious preservatives Avoids hazards of transmission of hepatitis virus.
Extremely rare immediate reactions. (Result of elimination of globulins.)	Occasional reactions due to pyrogens or to increased plasma volume.
Concentrated albumin is only as viscous as is whole blood with a hematocrit of 50 percent.	When injected, lowers viscosity of blood due to hemodilution.

TABLE VI. CLINICAL STATES IN WHICH SERUM ALBUMIN IS USEFUL.

1. Shock.
2. Hypoproteinemia.
3. Hypoalbuminemia.
4. Chronic renal disease (nephrosis)
5. Acute renal failure.

(continued from page 94)

crease in circulating cells: the resulting anemia demands a more rapid circulation of existing hemoglobin to provide oxygen for the tissues.

Concentrated serum albumin has been distributed in 25 per cent solution for convenience, but it need not be given in such concentrated form and, indeed, it has been shown that the administration of additional saline enhances the effect of albumin. Although, because of its low viscosity, concentrated albumin is not harmful in the presence of dehydration, it is apparent that in patients suffering from shock and from depletion of fluids, or of fluids and electrolytes, the restoration of blood colloids will not completely restore circulatory balance. Since a 5 percent solution of albumin in physiological saline is approximately isosmotic and isotonic with citrated human plasma, it is desirable in the treatment of shock to supplement every 100 cc. of 25 percent albumin solution with from 400 to 500 cc. of saline solution.

HYPOPROTEINEMIA (6). Concentrated salt-poor albumin appears to be the ideal agent for the treatment of hyproproteinemic edema at those times when it is important to relieve the edema promptly, e.g., in pulmonary congestion or circulatory failure with oliguria. As a rule, however, hypoproteinemia is the result of a variety of factors: Inadequate protein intake, excess protein loss and increased catabolism due to disease or illness. When relief of hypoproteinemia is not urgent, the preferable method of treatment is to supply abundant amounts of dietary protein, orally supplemented as necessary by oral or parenteral administration of amino acid mixtures or hydrolyzed proteins. The use of plasma has the disadvantages that the protein administered is accompanied by relatively large amounts of water and of sodium, that the protein content is only half albumin (which has the greatest osmotic value), and that an occasional case of homologous serum jaundice will occur. However, serum albumin, in the relatively few cases in which it has been used, elevates the serum albumin level in the blood rapidly and produces a prompt diuresis even after parenteral protein mixtures have failed.

In general, the following rules should be observed in utilizing serum albumin:

1. Maintain a high caloric intake, high in protein, to avoid drawing on the serum albumin for energy.

2. Serum albumin should be given in adult daily doses of 50 grams, either in two doses, or by continuous intravenous infusion with 200-300 cc. 10 percent glucose.

3. Much more serum albumin must be given than is indicated by the deficit in circulating albumin.

4. Injected albumin will not appear in the urine unless proteinuria already exists.

HYPOALBUMINEMIA. In diffuse diseases of the liver with the commonly associated hypoalbuminemia, the serum albumin can be brought back to normal, peripheral edema lost and some degree of improvement in ascites obtained in 7 to 14 days by the administration of 25 to 50 grams of serum albumin a day intravenously in addition to an adequate diet. In irreversible conditions, such as advanced cirrhosis, cessation of albumin therapy is usually accompanied by clinical relapse; in reversible liver disease, such as acute hepatitis, improvement is permanent.

CHRONIC RENAL DISEASE (NEPHROSIS) (7). Reduced colloidal osmotic pressure is an important factor in the formation of the edema of chronic nephrosis and serum albumin would appear, therefore, to be the ideal diuretic agent. However, diuresis does not always follow administration of albumin to these patients and massive doses over

long periods of time are often necessary to produce diuresis. Furthermore, a large percentage of the albumin so administered is excreted in the urine within 48 hours and there is some reason to believe that albumin so administered produces renal damage. However, a trial of serum albumin is certainly indicated in those patients who have not responded to other measures.

ACUTE RENAL FAILURE (8). Pursuant to the theory that the best treatment of anuria is to maintain the chemical balance of the circulation by parentereal therapy and to support the patient until the excretory function is restored, serum albumin is indicated both in those cases of acute renal failure in which hypoproteinemia is an important etiological factor and also in primary renal failure such as is encountered in acute nephritis and in sulphadiazine intoxication.

GAMMA GLOBULIN

Separation of the gamma globulin fraction of blood plasma provides the major portion of the antibodies present in the plasma in a concentration approximately twenty five times that in normal pooled plasma. When gamma globulin is obtained from pools of plasma from large numbers of blood donors there is a rather uniform titer of antibodies against the infectious agents endemic to the geographic area in which the donors reside. The presence of such antibodies appears to depend upon both clinical and subclinical (inapparent) infections. The uniformity of antibody levels in pooled plasma and consequently in gamma globulin depends chiefly upon three factors: (1) Presence of endemic or of recent epidemic disease in the area from which the blood is drawn, (2) Amount and duration of antibodies resulting from specific infections, and (3) Number of donors contributing to the pool. The presence in gamma globulin of concentrated antibodies which will passively protect against measles, mumps and infectious hepatitis has been studied in humans. Information relative to poliomyelitis is largely the result of animal studies.

MEASLES (9, 10). Gamma globulin appears to be the most satisfactory biological agent as yet developed for the passive protection of exposed susceptibles, or for the attenuation of the disease. There is considerable assurance that the globulin in general has a constant titer of measles antibodies. Less certain is the value of gamma globulin in the treatment of early cases of measles, although it is likely that the disease may be modified if globulin is administered during the prodromal period.

MUMPS (11). Apparently gamma globulin from plasma pools derived from the general population is not usually effective in protecting exposed susceptibles against mumps when administered in amounts up to 50 cc. More valuable globulin for this purpose might be obtained from the pooling and fractionation of large amounts of convalescent plasma. If such globulin could be obtained, it would seem desirable to reserve its use for adult males in the first 24 hours of their illness with the purpose of preventing or attenuating acute orchitis.

INFECTIOUS HEPATITIS (12, 13, 14, 15). It has been demonstrated convincingly that gamma globulin in doses of 10 cc. will confer passive immunity to infectious hepatitis (epidemic hepatitis) for periods from six to eight weeks, but gamma globulin apparently has no value in the treatment of active cases. It is unlikely that gamma globulin would be as effective in serum hepatitis as it is of the infectious type.

POLIOMYELITIS (16). In animals, treatment with gamma globulin has been totally ineffective and injections of large amounts of gamma globulin during the incubation period has not modified the severity of the disease produced

by intracerebral inoculation. During an epidemic of poliomyelitis among humans, large doses of gamma globulin were injected parenterally as treatment in pre-paralytic cases, but had no demonstrable effect on the course or outcome of the disease.

RUBELLA. There is no adequate data available upon which to assess the effect of gamma globulin on German measles, but in several isolated instances persons presumably susceptible and intimately exposed to cases of the diseases did not become ill after given gamma globulin. The importance of gamma globulin in this ordinarily benign disease lies in its use for women during the first three months of their pregnancy, to prevent German measles and resultant fetal congenital deformities.

PROTEINS IN BLOOD COAGULATION

There are three groups of proteins, occurring naturally in the blood plasma, some in the form of precursors, which enter into specific stages in the blood clotting mechanism. These may be tabulated and are discussed in Table VII.

FIBRINOGEN AND FIBRIN

Fibrinogen, a plasma protein synthesized in the liver, occurs in the plasma to the extent of approximately 0.28 percent. By the method of fractionation employed at Harvard, the major portion of the fibrinogen is concentrated in Fraction I. In Fraction I prepared as a dry sterile powder, the fibrinogen remains stable for an indefinite period of time. The fibrinogen molecule is larger than that of any other plasma protein, the molecular weight being in the neighborhood of 500,000. Both fibrinogen and fibrin possess a molecular structure analgous to the fibrous proteins, keratin and myosin. Apparently there is no fundamental difference in the detained molecular pattern of fibrinogen and fibrin and the process of clotting seems to involve the linking of fibrinogen molecules into far longer needle-like microcrystals which represent the fibrin molecule. The nature of the transformation of fibrinogen into fibrin is still not entirely clear.

By reason of its fibrinogen content, Fraction I, in combination with human thrombin derived from Fraction III, has been used by surgeons to promote the adhesiveness of skin grafts (17), and to form coagulums around renal calculi to facilitate the removal of these calculi without fragmentation (18). In the form of fibrin foam with thrombin, these proteins are used to accomplish rapid hemostasis in neurosurgery and in general surgery (19, 20). Fibrin films provide pliable, transparent and yet relatively tough membranes which can be used as a framework for the ingrowth of connective tissue without the hazard of adhesion formation.

PROTHROMBIN AND THROMBIN.

Prothrombin is a euglobulin containing about 4 percent carbohydrate. It is found in Fraction III-2 in a highly concentrated form. It can be converted to thrombin by interaction with tissue thromboplastins derived from brain,

TABLE VII. PLASMA PROTEINS ENTERING INTO BLOOD CLOTTING MECHANISM

I. Substances forming the structural basis for the clot.	Fibrinogen Fibrin
II. Substances concerned with inducing clot formation.	Thromboplastin Prothrombin Thrombin Globulin substance which promotes coagulation of hemophilic blood.
III. Substances which dissolve the fibrin clot.	Fibrolysins.

lung, placenta or other tissues. The thrombin so formed can be used on sterile gauze, on fibrin foam, or on absorbable cellulose and applied with pressure to bleeding points. Theoretically prothrombin administered parenterally is the ideal treatment for patients who exhibit a prothrombin deficiency, but, practically, the danger of its promoting intravascular clotting is too great. Most available prothrombin preparations are relatively unstable.

Thrombin is a euglobulin much like prothrombin but more stable. It can be made into a solution which, when filtered, frozen and dried, is stable over long periods of time, Thrombin is an excellent topical hemostatic. For open wounds, thrombin from animal sources may be used without fear of local or systemic reaction. An extremely potent hemostatic agent available commercially under the name of "Hemostatic Globulin" is made from animal sources and requires no activation by thromboplastin. For wounds which are later to be covered by suture, preparations of human thrombin and absorbable nonreactive sponges are necessary. The introduction of such hemostatics has undoubtedly reduced the dangers of surgery, especially those attendant upon surgery in hemophilic patients. Thrombin preparations must never be used intravenously because of the hazard of intravascular clotting and shock.

THROMBOPLASTINS. Thromboplastins are lipoproteins which are obtained from various tissues and which, in the presence of diffusible calciumions, convert prothrombin into thrombin. Commercial preparations are used in the laboratory to activate prothrombin in the determination of the prothrombin time; clinically, they are used as local hemostatics.

GLOBULIN SUBSTANCE. There has been isolated from plasma a globulin fraction which accelerates the clotting of hemophilic blood (21, 22). It is a euglobulin, distinct from thromboplastin, prothrombin and thrombin. It is found in Fractions I and III-2 and is thermolabile. It is hoped that when concentrated and standardized, it will be available commercially for the preparation of hemophilic patients for surgery.

FIBRINOLYSIN. A fibrin clot slowly dissolves even under sterile conditions, the process requiring a period of some hours to a matter of weeks depending upon physico-chemical conditions. This process of dissolution of a clot may be accelerated by the addition to it of Fraction III-2 or of thrombin prepared from this fraction. The active factor, fibrinolysin, is a heat-labile proteolytic enzyme which may play a role in the initiating of clotting by serving as the active agent in the conversion of prothrombin to thrombin.

ISOAGGLUTININS. Anti-A and Anti-B isogglutinins and Anti-Rh globulins are obtained from Fraction III-1 by concentration from pooled group specific or anti-Rh plasma. These are potent and dependable reagents useful in the laboratory for the grouping of blood for transfusion.

OTHER PLASMA PROTEIN FRACTIONS. There have also been isolated specific plasma globulins which combine reversibly with iron and presumably transport it to the tissues, which dissolve water soluble lipids, such as cholesterol, vitamin A and estriol, and which have enzymatic actions. Plasma albumins have been shown to combine selectively with organic metal complexes, such as mercurials and sulphonamides, and with water insoluble organic molecules, such as quinones and long chain fatty acids. Thus there is evidence that the further fractionation of plasma proteins will isolate products whose interactions in the blood and tissues are of profound physiological

significance in the human organism in health and disease.

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A New Jet Method of Nasal Medication

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"THE question of sterility of solutions for intranasal use is important and there is an answer. The answer does not lie in avoiding the issue by the use of stronger antiseptics. It lies in sterile solutions correctly dispensed and correctly used."

Thus did Gompertz and Michael[1] comment five years ago when they proved that "repeated contamination of nose drops in dropper bottles results in their supporting living bacteria". The challenge of their comment has gone unanswered, except by education, instruction and care.

Correct dispensing of nasal medication is difficult because of contamination from droppers by means of which solutions are commonly used, and the correct use of droppers is difficult to teach and inconvenient for the patient to carry out. When atomizers are employed for use of the medication, contamination can occur from mucus on the applicator tip, when liquid is sucked back into the reservoir. The medication is not clinically as effective as it should be in either case because of the difficulty of placing measured amounts of medicament high in the nose. Clearly, a new device is needed—one which makes nasal medication safe from contamination and effective.

Study of the dropper was made by x-ray, using a solution which is opaque to the radiation. Figure I shows that the patient using a medicine dropper has succeeded in introducing the solution into his nostril from the dropper tip, and that the liquid is wetting the

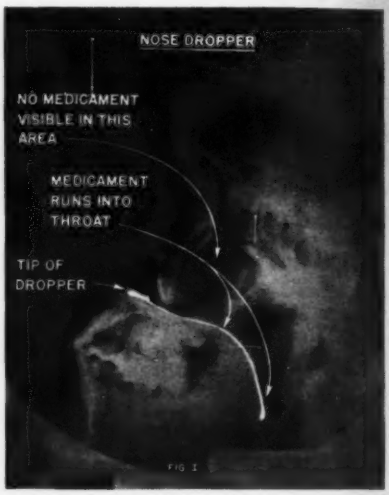

Fig. 1. X-Ray of Nose Dropper Method of Nasal Medication.

floor of the nasal cavity, but the drops have not been instilled high enough to wet the upper sinus area. By better technique and the use of the Parkinson or Proetz positions the distribution of the fluid could have been improved.

A similar x-ray study of the atomizer shows the same patient using the x-ray opaque solution with somewhat better results. No medication, however, is visible above the lower surface of the middle turbinate, and no droplets of the solution are to be seen in the upper sinus areas, where medication is desired. These results are shown in Figure II.

To reach the upper sinus areas, working against gravity, it is necessary

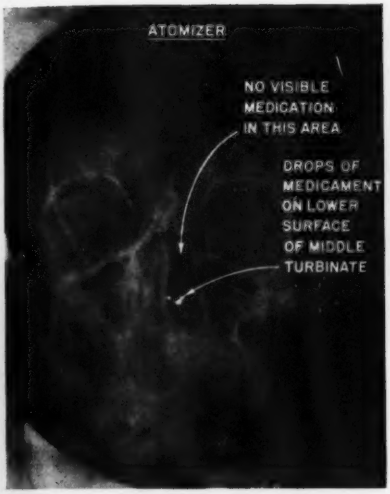

Fig. 2. X-Ray of Atomizer Method of Nasal Medication.

Fig. 3. X-Ray of Jet Applicator Method of Nasal Medication.

to positively instill the medication in the form of a fine jet. Figure III shows the effect of introducing a tiny stream of x-ray opaque liquid by pumping it through the orifice of a nostril-engaging applicator. The liquid goes high into the nasal cavity and spreads over the mucosa where medication is desired.

The device which was developed to jet the medication as shown in Figure III is compact, constructed of plastic so that it will not break or corrode, is almost self-directing even in the hands of a child, and delivers a measured dose of 2 or 3 drops at each stroke of the positive displacement pump which supplies the liquid to the jet. It is pictured in Figure IV.

"The question of sterility of solutions for intranasal use is important—", and—"it would appear that vasoconstrictor solutions in dropper bottles are probably sterile as dispensed by the pharmacist".[1] Correct dispensation of the solutions is accomplished with the new device by merely pouring the sterile medication into the plastic bottle of the device. Once pumped from this bottle, two valves prevent the solution from returning and contaminating the medication. Correct use of the medication involves merely inserting the applicator tip in the nostril, jetting the prescribed dose, and then carefully wiping the applicator tip with an antiseptic.

The fact that the method of dispensing and correctly using medication in the new device presents a minimum hazard from the standpoint of introducing complicating organisms into an already infected area was shown by a series of cultures, in which the medium used was brain heart infusion in order to grow even the more fastidious microorganisms. Tests were conducted on patients selected at random, and who had been using the new device for medication as prescribed. The information obtained is tabulated in Table I.

From this information it is apparent that organisms are readily transferred from the nostril to an applicator; that the applicator may be effectively cleaned by careful swabbing with 70

percent alcohol; that cleansing the applicator with soap and water is not sufficient to wash away contaminating organisms; and that the medicine in the new device remains uncontaminated. In the one case where contamination is indicated, the growth was traced to faulty technique in obtaining the sample, as subsequent cultures were negative.

Conclusions

1. A new nasal applicator[2] has been developed which is safe from contamination, and effective in placing medicaments high in the nose.
2. Sterile nasal medication dispensed by the pharmacist need not be contaminated when used by the patient in the new device.

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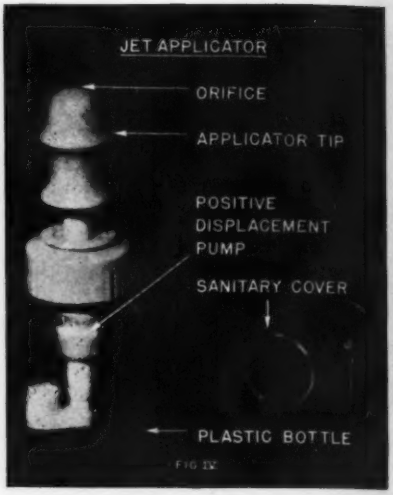


Fig. 4. Jet Applicator.

TABLE I.

Patient	Culture from Nose	Culture from Medicine In Device	Not Cleaned	Cultures from Applicator Tip Cleaned with Soap, Tap water, and steril brush	Cleaned with swab, 70% Alchohol
R. F.	Growth	No Growth	Growth	No Growth	
N. F.	Growth	No Growth	Growth	No Growth	
F. W.	Growth	No Growth	Growth	No Growth	
K. C.	Growth	Growth	Growth	No Growth	
M. F.	Growth	No Growth	Growth	No Growth	
M. M.	Growth	No Growth	Growth	No Growth	
B. B.		No Growth	Growth		Growth
A. O'S		No Growth	Growth		Growth
N. H.		No Growth	Growth		Growth
A. M.		No Growth	Growth		No Growth
C. H.		No Growth	Growth		Growth

DISCUSSION

This material on this new type of atomizer is interesting but it should be remembered that no local application is of any permanent curative value and should not be used regularly.

Since the work of Hansel, we know that 90 percent of nasal symptoms are allergic rather than due to "sinus" and follow dietary indiscretions, changes in weather, inhalation of chemicals, pollen and other materials to which the patient is sensitive.

The material if bacterial culture is pseudoscientific. Everyone has bacteria

in the nose and throat, but they are not pathogenic, i.e. will not cause disease. This is especially true of staphylococci which may be found on the skin and elsewhere.—Ed.

DISCUSSION

The editor was perfectly right in his criticism when he said the bacterial work was incomplete. This was purposely so, as there was nothing new to be found in the ordinary culture from the anterior nares or the nasal cavity. The purpose of our work was a gross check (see Table I) to see whether soap and water, which we had supposed would cleanse the nasal applicator sufficiently so it could be used by another member of the family. Our check showed this was not sufficient, but that it was safe when swabbed with 70 percent alcohol. The other part of the table shows the valves into the pump of the Jetomizer prevented any sucking of the secretion from the nose down into the Jetomizer bottle.—F. M. TURNBULL, MD.

TABLE II

(Same as Table I but Showing Types of Growth)

Patient	Culture from nose	Culture from Medicine In Device	Not Cleaned	Cultures from Applicator Tip Cleaned with Soap, Tap water, and Sterile brush	Cleaned with swab, 70% Alcohol
R. F.	N. catarrhalis Staphylococcus albus	No growth	N. catarrhalis		No growth
M. F.	Staph. albus	No growth	Staph. albus		No growth
F. W.	N. catarrahalis B. subtilis	No growth	N. catarrhlis B. sugtilis		No growth
K. C.	N. catarrhalis Pneumococci (Not typed)	N. catarrhalis Penumococci (Not typed)	N. catarrhalis Pneumococci (Not typed)		No growth
M. F.	N. catarrhalis Strept. gamma	No growth	N. catarrhalis Strept. gamma		No growth
M. M.	Staph. algus N. catarrhalis	No growth	Staph. albus N. catarrhalis		No growth
B. B.		No growth	N. catarrhalis B. subtilis	N. catarrhalis B. subtilis	
A. O'S.		No growth	N. catarrhalis Strept. gamma	N. catarrhalis Strept. gamma	
N. H.		No growth	Staph. albus N. catarrhalis	Staph. albus N. catarrhalis	
A. M.		No growth	N. catarrhalis Staph. albus	No growth	
C. H.		No growth	C. pseudo-diphthericum. Staph. albus	C. pseudo-diphthericum. Staph. albus	

There is no sound distinction between prevention and cure, except that prevention is a cure really effected in time and that so-called cure is often delayed prevention.—C. E. A. WINSLOW

Hippuric Acid Liver Function Test

By ARMAND J. QUICK, M.D.

Professor of Biochemistry, Marquette University School of Medicine, Milwaukee, Wisconsin

Procedure of the Oral Test: Before the test, which should preferably be given in the morning about one hour after a light breakfast, the patient is instructed to empty his bladder as completely as possible. The urine obtained is discarded. A dose of 3 gm. of sodium benzoate dissolved in 15 cc. of water (flavored with oil of peppermint if desired) is taken orally followed by a half glass of water. One half hour later a second dose of 3 gm. sodium benzoate is taken and followed by a half glass of water. By taking the sodium benzoate in divided doses, nausea is greatly reduced. One hour after the initial dose is taken, the complete specimen of urine is collected. The second, third and fourth hour specimens are likewise collected.

Each hour specimen is measured in a graduate. If the volume of any one hour exceeds 150 cc., it is advisable to acidify the urine slightly with acetic acid and concentrate it on a water bath to about 50 cc. Each specimen is made neutral or slightly alkaline with a drop of ammonium hydroxide. Solid ammonium sulfate is added in the proportion of 5 gm. to every 10 cc. of urine. When the salt is dissolved, the urine is filtered, and then strongly acidified with concentrated hydrochloric acid until acid turns to Congo red or thymol blue (pH about 2). Usually about 1 cc. of hydrochloric acid is sufficient. The solution is vigorously stirred and the sides of the beaker scratched with the stirring rod to promote crystallization of the hippuric acid. After standing 15 to 30 minutes, the hippuric acid is filtered by suction. A convenient way is to use a 25 mm. porcelain filter plate fitted into an ordinary funnel and covered with a 4.25 cm. filter paper. After the precipitate is washed with sufficient cold water to remove all the ammonium sulfate, the hippuric acid is dried and then weighed without removing it from the filter paper. As counterweight, another filter paper of the same size is used. The hippuric acid can also be determined by titration with standard sodium hydroxide using phenolphthalein as indicator. The hippuric acid is transferred to a beaker, water and a few drops of the indicator added, and the solution heated nearly to boiling before titrating with 0.5 N sodium hydroxide. Since 1 cc. of 0.5 N sodium hydroxide is equivalent to 0.0895 gm. hippuric acid, the titration in cc. x .0895 gm. is equal to the hippuric acid in sample. To this must be added the quantity of hippuric acid remaining in solution. The solubility of hippuric acid in the concentration of ammonium sulfate used is 0.001 gm. per cc. of urine, therefore urine volume x 0.001 = gm. of hippuric acid remaining dissolved. The latter value is added to the hippuric acid determined either gravimetrically or volumetrically to get total hippuric acid output. To convert the amount of hippuric acid into the amount of benzoic acid it represents, one multiplies by 0.68.

The Intravenous Test. It is best that the test be done in the morning an hour after the patient has had a light breakfast. A solution containing 1.77 gm. of sodium benzoate (equivalent to 1.5 gm.

of benzoic acid) in 20 cc. of distilled water is given intravenously. This solution is prepared with the usual precautions taken in making any preparation intended for intravenous use.* The injection should require 5 minutes or more. If the solution is given faster, the patient is apt to experience a pain in the upper arm. The patient voids before the test, and completely empties his bladder exactly one hour after the injection. In order to increase the volume of the urine, it is advisable to have the patient drink a glass of water a short time before the injection. The hippuric acid is determined in the same manner as the oral test.

* Ampules of sodium benzoate suitable for the intravenous test have been prepared by Hynson, Wescott, and Dunning, Baltimore, MD., by George A. Breon Inc., Kansas City, Mo., and Kremers Urban Co., Milwaukee, Wis.

The average healthy adult will excrete from 3 to 3.4 gm. of benzoic acid as hippuric acid under the conditions of the oral test. For convenience 3 gms. is chosen as the average normal for calculating the output in terms of per cent of normal. On this basis an excretion over 90 per cent is considered nonpathological. It is likely that an excessive excretion, i.e., over 120 per cent is not normal, but at present it is not possible to explain such results. The output of hippuric acid in the intravenous test has been found to range from 1.0 to 1.4 gm. (equivalent to 0.7 to 0.95 gm. of benzoic acid). Since 1 g.m. of hippuric acid can be accepted as the minimal normal output, it is unnecessary to convert the weight of the hippuric acid to benzoic acid for calculating the per cent of normal as it is done in the oral test.

Penicillin in Postpneumonic Empyema

Earlier reports on the use of penicillin in the treatment of empyemas were quite optimistic and gave promise that it might be possible to avoid surgical drainage in a larger group of cases. Keefer first reported the now well-established fact that empyemas can be sterilized by penicillin and several groups reported the successful clinical cure of series of patients in whom only an occasional patient required surgical intervention. More recently J. K. Poppe (*J.A.M.A.*, 129, 435, Oct. 6, 1945) studied thirty-eight patients who had developed empyemas while receiving adequate penicillin therapy and all but two of these required surgical drainage. B. Blades (*Trans. South. Surg. Assoc.*, 56, 288, 1944) has also reported the need for surgical drainage in a high percentage of empyema patients in spite of penicillin therapy. R. Cohn and W. Luttgens (*Stanford Med. Bull.*, 5, 27, February 1947) report experiences with twenty-eight empyema patients treated with aspirations and local and parenteral administration of penicillin. Only ten patients made an immediate recovery under this regime, the remainder requiring subsequent surgical drainage. Even though penicillin may sterilize the pleural fluid and cause the patient to appear clinically well, the fluid should be drained completely and delay in drainage leads to progressive thickening of the pleura complicating later surgery.

Abdominal Distention

A normal abdomen is scaphoid and does not extend above the level of a line from the sternum to the public bone (Fig. 1). When the abdomen extends above this xipho-pubic line, distention of some degree is present (Fig. 2). Repeated measurement of the abdominal girth at the umbilicus with a steel tape may be used to record the distention and its progress. (Fig. 3).—WILLIAM HENDRICKS, M.D. (Northwestern University Medical School, Chicago) in *Surg. Clin. N. Am.*, Feb. 1947.

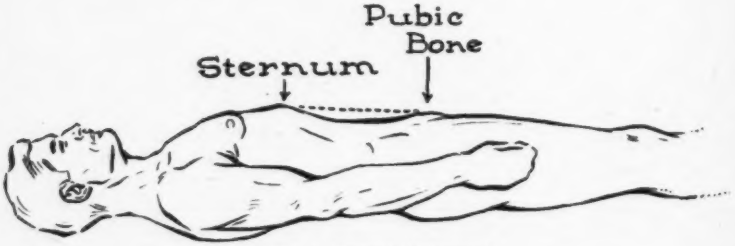


Fig. 1. Normal Abdomen.

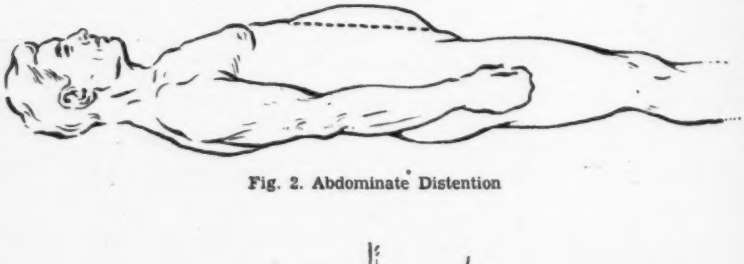


Fig. 2. Abdominate Distention

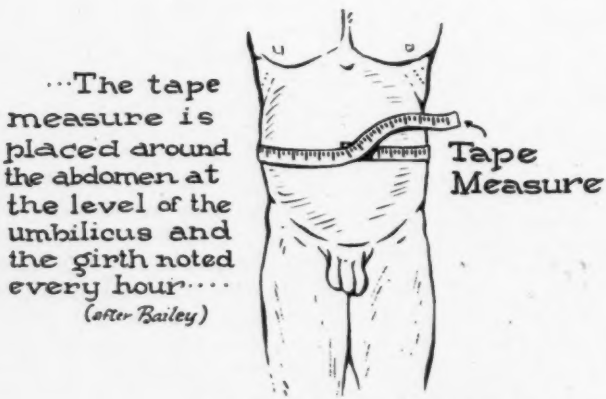

...The tape measure is placed around the abdomen at the level of the umbilicus and the girth noted every hour....
(after Bailey)
Tape Measure

Fig. 3. Measuring Abdominal Distention.

Fluctuation: Testing for Pus

Question: What is a simple dependable method of testing for pus in a superficial swelling, such as large abscess or boil? M. D. Denver, Colo.

Answer: Fluctuation is the name given to the sign of fluid. It does *not* specifically denote pus, but if signs of inflammation are present one may assume that the fluid is pus.

Hamilton Bailey's book "Physical Signs in Clinical Surgery" (John Wright & Sons, Bristol, England) gives several helpful suggestions and photographs, from which these sketches were adapted.

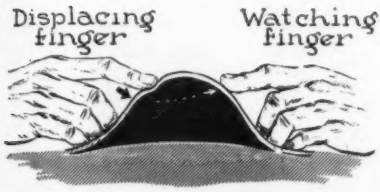
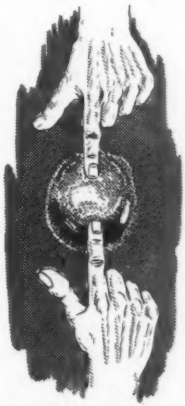


Fig. 1. The index fingers are placed on opposite sides of the center of the swelling. One finger gently depresses the swelling (displacing finger); the other finger is kept still (watching finger). If fluid is present, the watching finger is displaced away. Several successive depressing motions causes a fluid wave sensation to be transmitted to the watching finger.



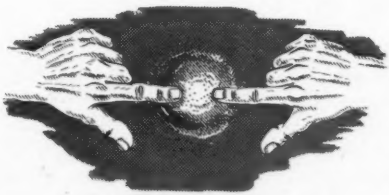


Fig. 2. Fluctuation is sought for in both axes of the swelling because: (See fig. 3)

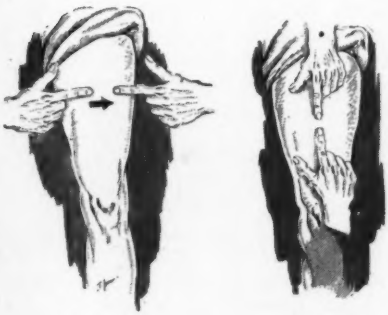


Fig. 3. Fluctuation is normally felt in one axis in certain tissues, such as transversely across the normal thigh, but not in the other axis.

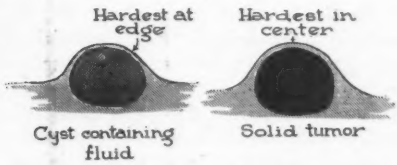


Fig. 4. Paget's test is based on the axiom that a solid is hardest in the center but a cyst is least hard in the center.

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Clinicopathologic Conference
(Case 13)*

History

A 64-YEAR-OLD man (Fig. 1) was admitted to the hospital because of *hemoptysis* and *abdominal pain*. Dull pain had been present in the right axilary region for 1 year. A gradual *weight loss* of 16 pounds occurred during the last 6 months, together with mild anorexia and malaise. Urgency, frequency and dribbling of urine present for 2 years, had become more intense.

Three weeks before admission and five hours after a hearty meal, he was awakened by severe, constant, periumbilical pain radiated to xiphoid and perineum, which persisted for 1 week and necessitated hospitalization. Vomiting appeared; nausea persisted. The pain shifted to the right upper quadrant where it remained. Stool habits and gross appearance of stools were normal. No fever appeared

Cystoscopy, retrograde pyelograms, gastrointestinal x-rays and barium enema showed no positive findings except a questionable blunting of middle renal calyxes on the right; intravenous pyelograms showed no visualization of the right kidney. X-rays of the chest showed "bilateral basal atelectasis and diminished excursion". A cough, with small hemoptyses, appeared.

Examination

Physical examination (Fig. 2) revealed a moderately well nourished man in no acute distress. Heart examination was negative; the breath sounds were diminished at the right base laterally, and fine rales and dullness were observed over this same area. Pain on respiration and a friction rub were noted on the left lower lateral chest. The abdomen and extremities were normal.

The temperature was 99.2°F., the pulse 100 and respirations 20; blood pressure 120/80. Urine: acid, specific gravity 1.017, positive albumin test, nu-

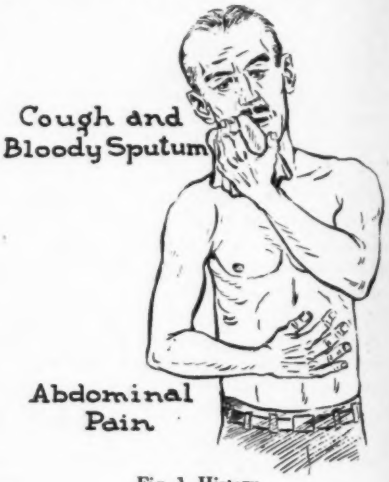


Fig. 1. History

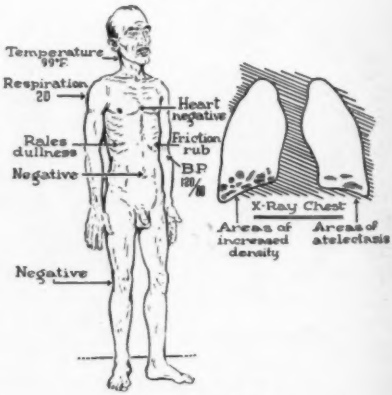


Fig. 2. Examination

* Adapted from the *New England Journal of Medicine*, Mar. 29, 1945; Case 31,131 of the Massachusetts General Hospital, Boston. Original illustrations by *Clinical Medicine*.

merous white cells and bacteria in sediment. White blood cell count was 11,100 with 92 percent neutrophils and 10.5 Gm. hemoglobin. Blood serum nonprotein nitrogen, protein and chloride examinations were normal.

X-ray: Retarded motion of both leaves of diaphragm, right more than left. Above them were linear areas of atelectasis at each base and on the right were patchy areas of increased density. There was little change in films taken three days previously. The right kidney could be visualized.

Course

The pain in the right chest increased on the first day (Fig. 3) respirations reached 35 per minute, the temperature increased to 102°F. The abdomen was distended, tympanitic and tense with questionable tenderness in the right upper quadrant. (The distention disappeared after an enema). At no time was there tenderness over the femoral veins, over the calves of the legs and unilateral enlargement of one of the legs never appeared.

Small amounts of blood streaked sputum were coughed up; repeated examination failed to reveal the tubercle bacillus, streptococcus or pneumococcus.

On the second day, the chest was better aerated (Fig. 4) and the respiratory rate returned to 20. The gallbladder was faintly visualized after the Graham dye was taken.

On the fourth day, a definite gallop rhythm was heard at the apex. Fever of 104°F. appeared and sulfadiazine was begun. The pulse varied from 100 to 120 and respirations from 25 to 35. (Fig. 5). Fresh blood was seen in the sputum. Chest puncture in ninth interspace on the right yielded 60 cc. of grossly bloody fluid containing 6000 lymphocytes and monocytes per cc. Costovertebral angle tenderness was noted and a catheterized specimen of urine showed occasional red cells and casts, many white cells, and Staphylococcus aureus was grown on culture. Blood nonprotein nitrogen and carbon dioxide determinations were normal.

On the sixth day, after penicillin, the patient felt better and the fever had fallen to 101°F. On the seventh day, he

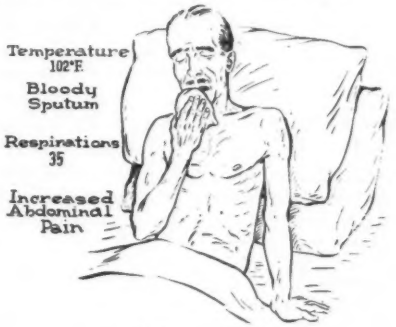


Fig. 3. Course, First Day

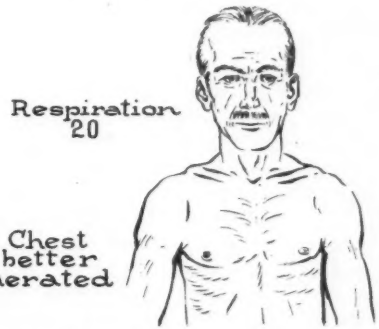


Fig. 4. Course, Second Day

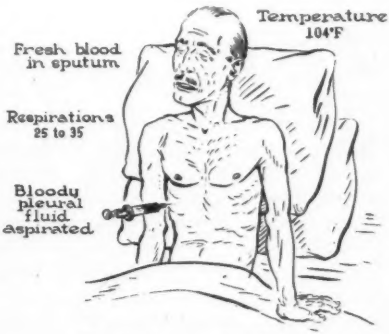


Fig. 5. Course, Fourth Day

became very restless, moaned, was in marked distress, began to gasp and expired shortly thereafter. (Fig. 6)

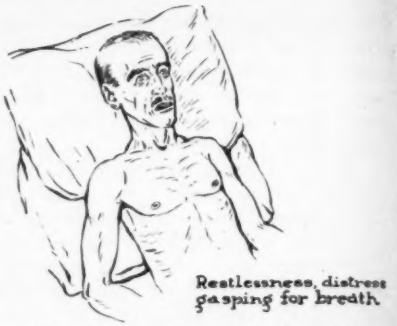


Fig. 6. Course, Seventh Day (Death)

Discussion

Chest pain, cough and raising of blood stained sputum are classic symptoms of pulmonary infarction (pulmonary embolism). Pneumonia occasionally causes acute abdominal pain, but the x-ray findings, white cell count and fever are not in keeping with it. Tuberculosis is ruled out because of x-ray findings and negative sputum tests. The bloody pleural fluid, weight loss and age of the patient make one think of metastatic malignancy.

Clinical Diagnoses: Pulmonary embolism; intra-abdominal infection of undetermined nature; tumor of right kidney with metastases to lung; pulmonary infarcts; terminal infection, bronchopneumonia or bacterial endocarditis?

Anatomic Diagnoses (Figure 7)

1. *Pulmonary embolism,* massive; 2. *pulmonary infarcts,* multiple, bilateral, recent and healing and 3. thrombosis of leg veins.

The cause of death was a large pulmonary embolus. Smaller pulmonary emboli had caused many small infarcts of the lung, in the lower thirds and along the diaphragm, with accompanying diaphragmatic pleuritis. The calf veins of both legs were the source of the emboli.

Bilateral pyelittis was present without any infection in the kidney substance.

Conclusion: Pain from lesions of the diaphragm can spread over the upper and lower abdomen. (Fig. 8). Bloody pleural fluid occurs in 10 to 15 percent of pulmonary infarcts. (This patient's life might have been spared if both femoral veins had been ligated or if he had been given dicumarol as an anticoagulant, under controlled conditions).

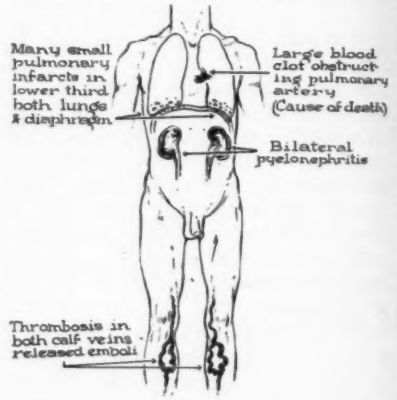

Many small pulmonary infarcts in lower third both lungs & diaphragm
Large blood clot obstructing pulmonary artery (Cause of death)
Bilateral pyelonephritis
Thrombosis in both calf veins released emboli

Fig. 7.

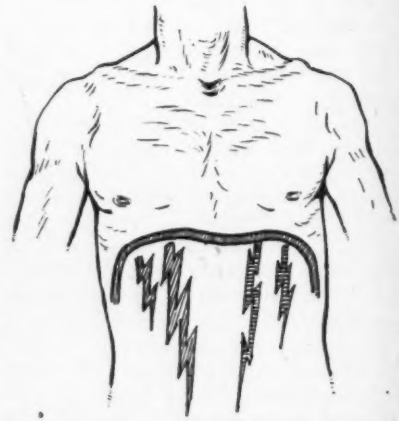


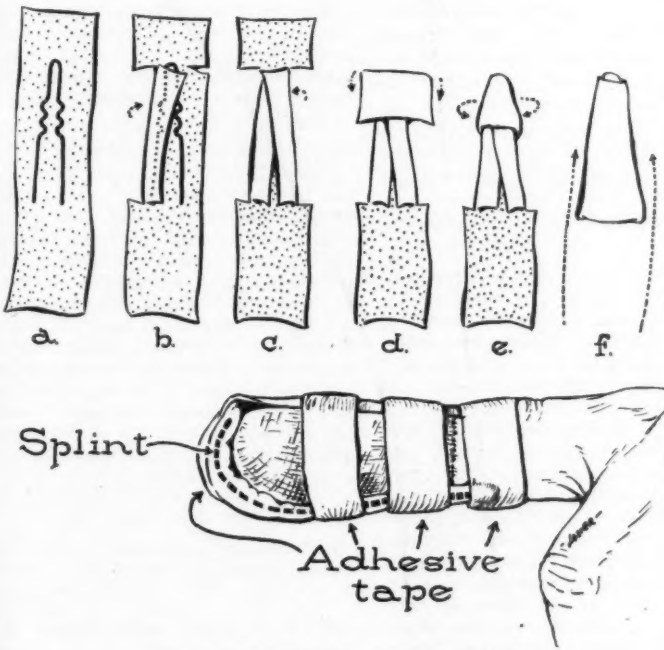
Fig. 8.

Problems in Practice

Finger Tip Infections

Question: What is a simple, inexpensive splint for the tip of the finger, necessary in the treatment of felons, paronychia, injuries and so on? M.D., Akron, Ohio.

Answer: The hairpin splint, as described by L. Kraeer Ferguson, M.D., of the University of Pennsylvania, Philadelphia, is always available, is simple to apply and need not be returned by the patient. The attached sketch is an adaptation of this author's technic, illustrating how the hairpin is covered with adhesive tape and molded to fit the finger tip. The dressing may be moistened as desired, without danger of its coming loose.



Hairpin Splint for Finger Tip Infections

Diabetic Pain in the Legs

Question: I have a diabetic patient who is well balanced in regard to blood sugars and urinary output of sugar, who has no anemia, no abnormal physical or laboratory findings but who complains of marked pain in the legs and "soreness" of the legs. What is the diagnosis and what can be done for the patient? H.K., M.D., New York City.

Diabetic Neuropathy

Answer: One of the more common complications of diabetes mellitus is involvement of the nervous system. W. R. Jordan (*Arch. Int. Med.*, 57,307, 1936) has classified the neurological complications into 4 groups: (1) Hyperglycemic, characterized by nerve and muscle tenderness without objective findings, found in patients with elevated blood sugar, responds well to treatment of diabetes; (2) Circulatory, in patients with arteriosclerotic changes; (3) Degeneration with impaired tendon reflexes and pupillary reactions; and (4) Neuritic, in which severe symptoms and signs appear in the legs acutely and respond slowly. O. J. Broch and O. Klovstad (*Acta Med. Scand.*, 127,514, 1947) studied 426 diabetic patients and found a somewhat similar grouping of neurological types.

The principal symptom of diabetic neuropathy is pain in the legs, often severe, especially at night, and accompanied by muscular tenderness. In advanced cases there is muscular weakness and atrophy, occasionally foot drop, loss of ankle and knee reflexes and impaired vibration sense. Loss of position sense in the feet leads to ataxia. Cutaneous sensory impairment, often dissociated in type, may involve the distribution of the spinal root segments rather than the peripheral nerves. A. Rudy and S. H. Epstein (*Journ. Clin. Endocrin.*, 5,92, 1945) noted evidence of spinal cord involvement in 26 out of 100 cases of diabetes with neurological changes. There may be tabetic-like disturbances of bladder function, usually associated with peripheral neuropathy (R. W. Rundles; *Medicine*, 24,111, 1945), but occasionally isolated.

Neuropathy is not the direct result of hyperglycemia or ketosis since it occurs in patients well controlled by diet and insulin (Broch and Klovstad). It may occur when the patient is maintained on a diet rich in vitamin B_1 (W. Needles: *Arch. Neur. Psychiat.*, 41,1222, 1939; H. D. Fein, E. P. Ralli and Joliffe. N: *J.A.M.A.* 115,1973, 1940) and treatment of it with large doses of vitamin B_1 does not accelerate recovery. A relation between diabetic neuropathy and peripheral vascular disease has been suggested but is not supported by clinical data (Broch and Klovstad; 22.5 per cent of patients with neuropathy have evidence of peripheral vascular disease; Rundles, 20 percent of patients with neuropathy have clinical evidence of peripheral vascular disease).

Treatment is obviously empirical since the pathogenesis is obscure. There is ordinarily a slow protracted improvement though calf pains, ataxia and impaired reflexes commonly persist permanently.

Peripheral vascular disease must be considered in a case such as this. Occlusive (arteriosclerotic) arterial disease will be manifested by reduced, or absent pedal and, perhaps, popliteal pulsations and by intermittent claudication. Arterial obstruction by thrombus or embolus will not only obliterate the pulses, but will reduce skin temperature and, perhaps, produce trophic changes or gangrene. Deep venous thrombosis (thrombophlebitis) will produce calf tenderness, possibly tenderness, redness, swelling and induration over the femoral veins and a positive Homan's sign (pain in calf on dorsiflexion of foot).

Reference

Annotations; Diabetic Neuropathy; Lancet (London) ii,626, October 25, 1947

C. D. MARPLE, M.D.

(Editor's Note: Subcutaneous injections of nicotinic acid may be of value. Sympathetic block of the affected side may be tried).

Treatment of Perforated Ear Drum

Question: I have a boy of 18 who has a hole in one ear drum. There is very little drainage, and flare ups of otitis media are rare. What prospects are there for closing the perforation in the ear drum?

Answer: A defect in the ear drum may close if tissues are stimulated by frequent acid cautery, removal of dried exudate, and application of urea solution. Results are best when the perforation is dry and surrounded by peripheral membranes, and deafness is not severe. The improvement to be expected in hearing is shown by closing the opening with a small paper splint or a cotton pledget soaked in gycerine.

Healing of the defect may relieve deafness, tinnitus, and may prevent recurrent ear infections. Anesthesia is obtained by brushing on equal parts of menthol, phenol, and cocaine, then applying a saturated solution of tri-chloracidic acid with a small copper or silverware hoop.

Cautery is repeated every week until granulation is satisfactory. If response to treatment is slow, 2 or 3 drops of saturated solution of urea is instilled once or twice a day.

Dried exudate should be remved twice monthly with a small hoop. The period of treatment may vary from one month to nearly two years. The younger the patient the better chance for sucecss but treatment may be effective after the age of 50.

The treatment should not be attempted if mastoid disease or middle ear disease is present, the bony chain is destroyed, the ear continuously discharges, tenth portion completely absent, or the tentanic membrane missing except for small fragments, or the eustachian tube obstructed.

Fatigue Allergy and Cigarette Smoking

Question: Many of my patients complain of being tired, yet examination by myself and specialists does not indicate disease nor do the symptoms become worse over a period of years. Am I overlooking a chronic allergy?—E. L., Los Angeles, Calif.

Answer: Fatigue without any physical or laboratory signs of disease is a difficult problem. The psychiatrists would have us believe that many such patients are the victims of an unresolved conflict—this is true in many cases, and yet all of us have certain things that bother us.

Food allergy is a common cause of fatigue (see Rinkel's article "Food Allergy" in *Clinical Medicine*, May 1947, for many clinical pointers), a fact that is not yet recognized by most internists and many allergists.

Coca in a recent article (Coca, Arthur F. "The Incidence of Idioblaptic Cigarette Sensitivity." Ann. Allergy, Sept.-Oct. 1947) describes a number of symptoms as being due to allergic sensitiveness to cigarette smoke: Fatigue, headache, loss of appetite, dizziness, constipation, indigestion, major and minor epilepsy.

Pruritus Vulvae During Menopause

Question: What is a simple, inexpensive treatment of pruritus vulvae during and after the menopause?—M. D., Chicago, Illinois.

Answer: Della Drips of the Mayo Clinic believes that simple, atrophic vulvitus and vaginitis with vulvar itching and a sense of soreness and congestion in the vagina should be treated by a 6 week course of estrogen, given orally, or in vaginal suppositories.

In cases of fatigue and tension ¼ grain of pheno-barbital is given after each meal and 1 grain at bedtime.

Corneal Ulcer

Question: I see many cases of foreign body injury of the cornea, a number of which are followed by ulcers of the cornea. As the nearest ophthamologist is 100 miles away, I usually give treatment to all those not requiring specialized attention. Are there any modern advancements in the treatment of corneal ulcers that I may carry on in my own practice in this isolated country?—M. D., Idaho.

Answer: A corneal ulcer occuring after a foreign body has been removed from the eye may be due to infection caused by the foreign body or by the instrument with which it is removed, or it may be caused by poor nutrition in the cornea. Such patients are improved by giving cod liver oil and using a Vitamin A ointment in the eye. Hot wet packs relieve pain and sometimes aid in healing.

The more direct application of heat was done in the past by a process known as pasteurization — this simply means that a heated metallic object is placed close to the eye after anesthesia has been obtained by cocaine three or four times over a period of 5 minutes. The object may be a small metal ball, a hot cautery point, or any other material that will radiate heat onto the eye's surface. It is held within 1½ to 2 inches of the eye, the lids having been widely spread apart. It should cause no pain at the time or later. The patients usually state that there is considerable relief of distress during or shortly after the heat has been applied.

Recently, Grossman has reported a series of resistant corneal ulcers which responded to the placing of human blood plasma or the patient's own blood into the eye every day (Archives of Ophthamology, June, 1947).

Bone Lesion

Question: I have a boy of nine with a bone lesion which is apparently a tumor. There is conflict between the roentgenologist and the pathologist who studied the material and removed the biopsy.

The roentgenologist feels from successive films that the lesion is not a sarcoma, but the result of injury. The pathologist feels that the lesion is a sarcoma and that the leg should be amputated. Please wire answer.—M. D. Des Moines, Iowa.

Answer: Amputation should never be carried out unless there is a clear cut evidence of malignant degeneration. The series of x-rays taken repeatedly at a few days intervals are much more accurate than one biopsy which often is not diagnostic.

James F. Brailsford, radiologist to the Queen Elizabeth Hospital, Birmingham, England, writes "I have not been fortunate enough to see a cure resulting from the prompt amputation of a limb showing a typical radiographic evidence of an osteogenic sarcoma. To amputate a limb where the radiographic and clinical evidence is not conclusive, even though the histologic changes suggest malignant disease, is to take an unjustifiable risk. If biopsy is excusable, it is so when it provides material which supports the clinical and radiographic evidence of simplicity rather than malignancy." He reports a number of cases of body changes due to syphilis, trauma, leukeumia, and so on. (Proceedings of the Royal Society of Medicine, of England, March 21, 1947).

Refactory Pernicious Anemia

Question: What medications may be used in cases of pernicious anemia which do not respond to repeated, large injections of liver extract.—M. D., Roswell, New Mexico.

Answer: If a particular brand of liver extract does not produce a therapeutic effect within two weeks, another should be used. A case should not be considered refractory until a number of preparations of liver or dried stomach have been thoroughly tried.

Editorials

American Specialty Boards: Trade Unions or Practice Betterment?

During the war years and increasingly since, many general practitioners and some thoughtful specialists have wondered about the outcome of the present rush to specialism.

The American Boards for each of the specialties have been of wonderful benefit in setting up standards and encouraging younger physicians to better preparation before entering upon a specialty. Unfortunately, some of the Board members feel that they know what is best for the whole profession and for all patients. Such men are recommending and even enforcing the principle that all hospital staff appointments of any importance should be held only by certified specialists.

Of this trend, Karl Martzloff states[1], "Membership in a society of specialists as an over-all prerequisite for recommendation to medical staff membership also eventually degenerates into the labor union principle of primary emphasis on membership and scant attention to ability, for here again such membership may bespeak only the most mediocre professional qualifications when put to the test of actual practice."

[1] Martzloff, Karl H.: Organization of the Hospital Medical Staff from the Standpoint of Maintaining a High Standard of Professional Proficiency. *West. J. Surg., Ob. & Gyn.*, Mar. 1947.

What the Boards State

Letters were written to the secretary of each Board asking if the board felt that every major appointment to a hospital staff should be restricted to Board certificate holders. Table I indicates the replies received by *Clinical Medicine.*

In all cases, the Board or its secretary felt that the certification method was the ideal method for obtaining the best trained men.

Will Diplomates Grow Stale?

Assuming for the moment that all diplomates, at the time of passing the Boards, are the best qualified men in their specialty, what is to keep them up to the intense pitch of study and research? The obvious answer would be to have a system whereby men who could not pass supplementary examinations each three to five years would be required to take postgraduate study or lose their certificates (this routine would be of value to all physicians, whether specialists or general practitioners). As yet, we know of no Board that thus keeps its diplomates on their toes in this forceful manner, and thus counteracts the human tendency to slow down.

Will the Boards Dominate Medicine?

As is well known, specialists dominate all medical organizations. It is only recently, for example, that the Ameri-

can Medical Association has even organized a section on general practice. Specialists dominate medical education and hospital appointments. It is only logical to assume that the Boards, who will soon certificate all specialists, will indirectly dominate the entire practice of medicine. In this way, a few self-appointed men can direct the entire team.

TABLE I.
Should Every Major Hospital Staff Appointment Be Restricted to Certified Specialists?

Board of	Yes	No	Desirable	Comments
Obstetrics Gynecology			X	"Certification distinguishes well qualified specialists from those who may not be."
Pediatrics			X	"Highly desirable"
Anesthesia		X		"Too few Diplomates now"
Otolaryngology	X			"If a man cannot qualify, he is not competent"
Surgery			X	"No official action taken to restrict appointments"
Dermatology Syphilology			X	"There is no better way of assessing training, capacity and competence"
Internal Medicine				"Impossible to give opinion"
Otolaryngology	X			
Pathology			X	
Psychiatry Neurology			X	"Man should be of caliber equal to that demanded by American Board"
Radiology			X	

A Specialty Board for General Practice?

Walter Bierring[2] suggests that general practitioners perform 85 percent of all medical practice, that something should be done to stimulate them with the same stimulus that is given to specialists and that a specialty board be set up to give them recognition as general practitioners.

Would such a board be another device for restricting the uncertified physician? Would enough general practitioners be interested, take the time and effort to make it worthwhile?

Clinical Medicine is asking a number of general physicians, as a test, the questions in the following opinionnaire. Your participation in this test survey would be helpful and appreciated. Fill out the Opinionnaire as completely as possible and mail to Clinical Medicine.

Replies from our mailings on this opinionnaire will be published in a later issue. If you have any ideas, suggestions or criticisms on what the American Boards are doing or on the establishment of a Board of General Practice, please tell them to us so that all may share in them.

[2] Bierring, W. L. Meeting of Committee for Postwar Medical Service. *J.A.M.A.*, page 41, Jan. 4, 1947.

CLINICAL MEDICINE .OPINIONNAIRE

1. Are you in favor of establishing an American Board of General Practice?

☐ Yes ☐ Undecided ☐ No

Those *favoring* the establishment of such a Board say:

A. "It will indicate to patients and the profession that I am interested in improving myself and giving the best possible medical care."

B. "It will increase our recognition in medical circles as well as from other groups. (Army, Navy, Veterans' Administration and Insurance Companies.)"

C. "I wouldn't be 'just another general practitioner'."

D. "It will give us clear cut standards of practice eliminating the confusion and lack of cooperation between specialty groups that we now have to contend with."

Those *opposing* the establishment of such a Board say:

A. "It would involve too much time and effort in study."

B. "The Diploma wouldn't mean much, for some time at least, in the matter of prestige."

C. "It would not be possible to cover all the fields involved in general practice."

D. "The Board might become a political instrument, placing unnecessary limitations upon the General Practitioner."

(Please check off, above, your reasons for or against.)

If you have other reasons, please give them below.

.....

.....

.....

2. Would you take a clinical examination by a Board of General Practice if it were given conveniently near your home?

☐ Yes ☐ Undecided ☐ No

3. In what fields are you now practicing? ☐ Obstetrics ☐ Minor Surgery

☐ General Medicine ☐ Urology ☐ Eye, Ear, Nose, Throat ☐ Pediatrics

☐ Major Surgery ....

(Others)

My age is: ☐ Under 30 ☐ 30 to 40 ☐ 40 to 50 ☐ 50 to 60 ☐ Over 50

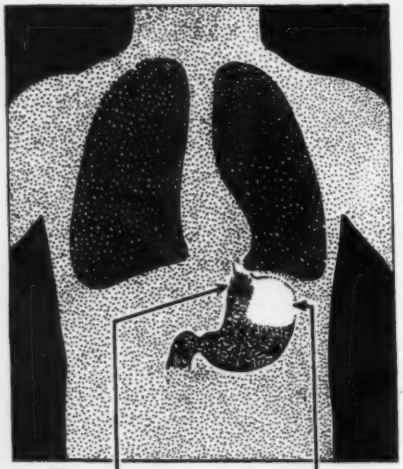
.....M.D.

.....

.....

(Please print or type)

DIAGNOSTIC POINTERS



Chest X-Rays Suggesting Gastric Cancer

X-rays of the thorax usually show the air bubble in the cardiac end of the stomach. If one examines the bubble closely, one may find a soft tissue mass projecting from the lesser curvature into the air-filled segment and thus suspect a carcinoma of the cardiac end of the stomach.—B. R. KIRKLIN, M.D. in *J. A. M. A.*, Aug. 9, 1947.

Diagnostic Error: Acute Intestinal Obstruction

An elderly male was admitted with a diagnosis of advanced acute intestinal obstruction. For three and a half days he had suffered from severe intermittent abdominal colic with persistent vomiting and had passed neither faeces nor flatus. He was collapsed and extremely dehydrated. Instructions were given for intravenous therapy to be followed in a few hours by laparotomy.

It was then observed, more by chance than good management, that the specific gravity of a sample of urine collected on his admission was 1.010. To check this surprising finding a catheter was passed and a mall sample of urine collected. The specific gravity was again found to be 1.010. The conditions for concentrating urine could seldom be as rigorous as these and yet these was no concentration.

Preparations for laparotomy were cancelled and intravenous therapy was given to correct the dehydration. In view of the kidney failure, care was exercised about the amount of salt to be given. The patient failed to respond and died. Autopsy showed gross *chronic glomerulonephritis* without any suggestion of intestinal obstruction.—M. COLE-ROUS, F. R. C. S., England, in *Clinical Proceedings*, Cape Town Postgraduate Med. Assoc., Sept., 1947.

Disorders of the Newborn

In an infant delivered by Cesarean Section, apparently normal at birth, who dies in 10 to 14 hours after progressive respiratory distress, post-mortem reveals an increase in fluid in the meingeal spaces and a progressive resorption atelectasis of the lungs.

An infant born a short time before estimated term, whose respiration is solely established after birth, and who becomes irregularly dyspneic and cyanotic, is usually found to have a liver-like consistency of the lungs due to capillary congestion, resorption of air, and presence of hyaline membrane surrounding

a few remaining air spaces. Death is forecast by the development of costal retraction with an increasing struggle for breath.

An infant born with a subcutaneous ecchymoses, mild edema, and a large spleen and liver, who lives only a few hours, is suffering from erythroblastosis.

An apparently normal infant who becomes jaundiced and dies after progressive anemia with increasing hypertonicity and tremors or actual convulsions is typical of kernicterus with staining of the basal nuclei of the brain with bile pigment.

An infant with a wide space between the eyes, a prominent epicanthic fold, a prominent cleft between the lower lip and chin, and large low set ears often does poorly. Death may occur within ten hours and be ascribed to complete renal agenesis.

When the chest of an apparently normal infant is occupied by an enlarged heart, or by viscera from the abdominal cavity or is compressed by upward pressure from polycystic kidneys, or when the trachea is closed by cartilaginous malformation, breathing may cease after a few futile attempts, despite initial vigorous beating of the heart. Efforts of resuscitation are futile.—EDITH L. POTTER, M.D., (University of Chicago, Chicago, Ill.) in *American Jrnl. of Clinical Pathology*, 17:524, 1947.

Asthma in the Aged

"Shortness of breath" varies as to cause and as to significance with advancing age. Attacks of primary asthma become less frequent as allergic susceptibility gradually wanes and the so-called asthmatic attacks in the elderly are secondary to serious organic disease, usually of the heart or kidneys—*Medical World*, Nov. 1, 1946.

The Adolescent "Problem" Girl

The adolescent girl who has a tendency to gain a little excess weight, slows up in mental processes, has difficulty in getting along in school, emotional disturbances and excessive movements resembling chorea, may be hypothyroid. A low basal metabolic rate is found and there is an encouraging response to thyroid extract given orally. Thyroid substance should never be given to relieve obesity unless thyroid hypofunction has been confirmed by metabolic rate determination. A. E. HANSEN, M.D. in *J. Missouri M.A.*, Feb. 1947.

Appendicitis vs. Renal Colic

If it is impossible to distinguish between early acute appendicitis and renal colic, perform intravenous urography at once. If the pyelogram shows a normal outline, an appendectomy should be performed.—HAMILTON BAILEY, F.R.C.S. London, (Eng.) in *Urologic & Cutaneous Rev.*, July 1946.

Peptic Ulcer and Achlorhydria

When a peptic ulcer is found in a patient who has no hydrochloric acid in the stomach, the ulcer is probably of a malignant nature.—ADOLPH SACHS, M.D.

Chronic Cervical Lymphadenopathy

The cervical region represents the cross-roads of tumor metastasis. Accurate differential diagnosis is essential to proper management and impossible without tissue examination. Differential includes: 1. Inflammatory vs. neoplastic lesion, 2. Benign vs. malignant neoplasm, and 3. Primary (intrinsic) vs. Metastatic vs. Generalized malignant process. Aspiration biopsy will sometimes suffice, but incisional biopsy is often necessary to establish a diagnosis.

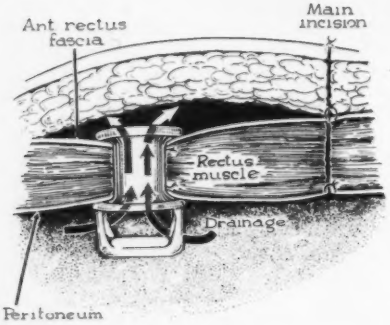
Peutic Ulcer: Therapeutic Test

A positive stool test for blood which persists after two weeks of a strict ulcer management indicates a probable malignant growth in the stomach or intestines if bleeding does not occur from the gums, nose or elsewhere along the intestinal tract.—ADOLPH SACHS, M.D.

Indigestion and Gastric Cancer

A change in diet habits or "indigestion" not responding to medical treatment should make one suspect carcinoma of the stomach.—ADOLPH SACHS, M.D.

Thumbnail Therapeutics



Drainage for Ascites

Ascitic fluid may drain out into the subcutaneous tissues through a surgically implanted hollow glass button (Roy C. Crosby and E. A. Cooney, Tufts College Medical School, Boston in *New England J. Med.*)

Head Injuries

Two surgical tests are indicated for the successful treatment of an open head injury: (1) the technical reduction of an open or compound injury to a closed or simple injury and (2) the prevention of infection.

The treatment of shock is given preference over all other treatment, except that of clearing the respiratory tract by aspiration and by maintaining a clear airway.

Unless there were signs of rapid deterioration, this period of resuscitation might be prolonged as long as 12 hours. Patients with active bleeding, uncontrolled by pressure dressings or by forceps applied to scalp arteries, with massive cerebral hematomas, with transventricular wounds and with a decreasing state of consciousness and an increase in neurologic signs, were considered candidates for immediate operative intervention.

Roentgen studies of the skull, in multiple projections and preferably stereoscopic, were, however, an essential part of the preparation for wound debridement.—Barnes Woodhall, Duke University School of Med., Durham, N. C., in *J.A.M.A.*, Nov. 29, 1947.

Penicillin for Infected Eyes

Penicillin may be obtained in high concentration in infected eyes by 1. dropping cocaine in the eye to produce local anesthesia, 2. injecting penicillin solution under the conjunctiva, every 5 or 6 hours, in doses of 50,000 units. The penicillin should be dissolved in equal parts of 2 percent procaine solution and adrenalin 1:1000.—Arnold Sorsby, M.D. in *Digest of Opthalmology*, Nov. 1947.

Folic Acid for Aplastic Anemia

The use of large doses of folic acid over long periods of time are of value to patients with aplastic anemia. The doses must range from 100 to 400 milligrams daily over a period of 3 or 4 months.—B. R. Gendel, M.D., in *Journal of Laboratory and Clinical Medicine*, Feb. 1947.

Ether for Asthma

One ounce, (30 cc.), of an equal mixture of ether and olive oil, or cottonseed oil, for every 20 pounds of body weight, is given as a retention enema every night for intractable asthma. A combination of the use of aminophylline in glucose intravenously during the day, and ether-oil at night, is an excellent one.—R. M. Balyeat, *Balyeat Hay Fever and Asthma Clinic Proceedings*, Oct. 1947.

Overweight

It is just as difficult to cure one of these individuals as it is to cure the habitual alcoholic. There is not the same social stigma attached to the unnecessary food that there is attached to the unnecessary gin.

Excellent studies of long term results of overwieght in group of over 22,000 army officers has been announced by Levy, White, Stroud and Hillman, et al. Their general finding was that transient hypertension or transient tachycardia or overweight, each by itself, increases the probability of the later development of sustained hypertension and its cardiovascular-renal disease. The presence of two of these conditions is of greater importance than any one alone. The presence of all three is a circumstance of major prognostic significance. These studies moved the overweight into the realm of the general practitioners as well as of the specialist who must deal with sudden complications in the chronically obese.

The large majority of people suffering from overweight do not regard it either as a catastrophe, nor of lamentable prognostic significance for their future lives.

Overindulgence in any phase of our living carries the potential of danger. The constant overload with the daily drag in the overweight needs must be dramatized, applied to the individual patient, and pounded upon day after day after day. In general it may be said that *only a few of the obese are patients suffering from glandular disorder. The large proportion simply have continued to eat as a growing child, with continued growth limited in the upper direction, but continued growth going on in all directions otherwise.*

Abdominal Injuries

The fundamentals essential in the operative management of abdominal trauma are (1) control of hemorrhage, (2) a thorough examination of all possible injuries involved, (3) accurate care of all hollow viseral wounds, (4) removal of all non-viable tissue and removal of foreign material, and, (5) drainage of the contaminated retroperitoneal space. —Pat R. Imes, M.D., Louisville, Ky., in *J.A.M.A.* Nov. 29, 1947.

Persistent Urinary Tract Infections

Persistent urinary tract infections, due to Pseudomonas aeruginosa and related organisms, responds to mandelic acid by mouth in doses of 3 Gm. four times daily (calcium mandelate), or methenamine mandelate two or three tablets give four times daily, if the urine is acid or can be made acid by administration of ammonium chloride or other acidifying agent. Streptomycin is most effective in an alkaline urine. Penicillin and the sulfonamides are of little effect.—Grayson Carroll, M.D. (Urology, St. Louis University Medical School, St. Louis, Mo.) in *J.A.M.A.*, Nov. 15, 1947.

Streptomycin for Tularemia (Rabbit Fever)

Streptomycin is effective in the treatment of tularemia, in intramuscular doses of 30,000 to 100,000 units every 3 hours. Total dose varies from 1,500,000 to 5,800,000 units.—Caldron Howe, M.D. in *J.A.M.A.*, Sept. 28, 1946.

The mortality and morbidity of tularemia are greatly decreased by streptomycin treatment. The diagnosis is established by positive cultures from local lesion or by blood agglutination reactions of increasing titer.—W. E. Herrell, M.D. in *J.A.M.A.*, Sept. 28, 1946.

Propylthiouracil for Hyperthyroidism

From 200 to 400 mg. of propylthioracil daily keeps many patients in a remission from hyperthyroidism for months. Patients with small or moderate sized diffuse goiters with mild or moderate hyperthyroidism, patients with recurrent hyperthyroidism and patients whose life expectancy is short, regardless of the type of goiter, may be safely given a trial on medical management for a year or more. If they respond favorably and prefer medical treatment, this may be continued indefinitely. If they respond poorly, do not cooperate or desire surgical removal, a subtotal thyroidectomy should be performed.—George Crile, Jr., M.D. in *West. J. Surg.*, Nov. 1947.

Surgery of the Ambulatory Patient

By L. Kraeer Ferguson, M.D., Professor of Surgery, Graduate School, University of Pennsylvania and Woman's Medical College, and L. Kaplan, M.D.—J. B. Lippincott. 1947. 2nd Ed. $10.00.

One of the few outstanding books in minor surgery today, primarily because it reflects the author's wide experience rather than being a collection of odds and ends collected from the literature. Anyone performing much surgery on office patients recognizes favorite technics that are successful, and more important, other technics which are very practical. The sketches and photographs illustrate diagnostic and therapeutic technic very well.

The only suggestion that could be made is in regard to the occasional statement made that some condition, such as severe nose bleed, be referred to a specialist if the recommended technic (a good one, by the way) fails. This advice is true if the specialist is close but the author has evidently never taken a patient two hundred miles in an ambulance to the nearest otolaryngologist. In the case of severe, peristant epistaxis, the simple suggestion of blood transfusion and packing the nose tightly with absorbable, oxidized gauze will control almost every case.

Let's Talk About Your Baby

By H. Kent Tenney, Jr., M.D., Associate Professor of Pediatrics, University of Wisconsin.—University of Minnesota Press. 1947. $1.50.

A little book written from the baby's standpoint, and with scientific child care emphasized.

Pathology of Labor, the Puerperium and the Newborn

By Chas. O. McCormick, M.D., F.A.C.S., Professor of Obstetrics, Indiana University.—C. V. Mosby. $8.50.

Complications and abnormalities of the delivery process are well illustrated, and described in this second edition. Modern therapy for the newborn is given in step-by-step form.

This is one of the most helpful practical volumes in obstetrics today because it: 1. tells how to recognize an abnormaility, and 2. shows exactly how to treat it.

Laboratory Manual of Microbiology for Nurses

By Elizabeth Gill, B.S., and James T. Culbertson, Ph.D., Assistant Professor of Bacteriology, University of Arkansas, Little Rock.—Putnam's Sons. 1947. $1.50.

In this course outline, the nurse is brought into contact with the destructive bacteria responsible for many of the diseases that she will aid in managing. The outline is simple to use, complete and clear.

Dermatologic Clues to Internal Medicine

By Howard T. Behrman, M.D., Assistant Clinical Professor of Dermatology, New York Univeristy College of Medicine.—Grune and Stratton. 1947. $5.00.

Alphabetically presented discussions of various internal diseases together with illustrations of skin manifestations which may occur in association with them. The text is clear, short, and up to date.

Epitome of the Pharmacopeia and National Formulary With Comments

American Medical Association Council on Pharmacy and Chemistry.—J. B. Lippincott. 1947. $2.00.

An ideal handbook for those who wish brief information on the chemistry, actions, and uses of drugs appearing in the U.S. Pharmacopeia and National Formulary.

The Story of Medicine

By Victor Robinson, M.D., Professor of Medical History, Temple University, Philadelphia. New Home Library. 1947. $1.00.

A simple, popular account of how medicine developed and of the great men who helped in its development. It is inspiring to the physician who tends to forget his mission in life.

Surgical Pathology

By William Boyd, M.D., Professor of Pathology, University of Toronto, Canada. W. B. Saunders. 1947. $10.00.

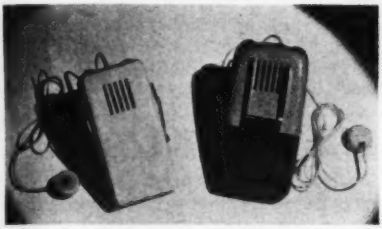
The gross and microscopic aspects of those diseases amenable to surgical therapy are well put forth. The literature has been well covered. Hundreds of illustrations aid in recognition of lesions.

Cancer

Diagnosis, Treatment, Prognosis. By Lauren V. Ackerman, M.D., Pathologist and Juan A. del Regato, M.D., Radiotherapist, to the Ellis Fischel State Cancer Hospital, Columbia, Missouri.—C. V. Mosby. 1947. $20.00.

A textbook of cancer, its recognition and management, written for the physicians and surgeons who must care for the great majority of such patients. It does not go into long discussions concerning minor points in treatmet. It does present related anatomy, pathology, clinical facts and technics of surgery and radiotherapy concerning each field and organ of the body. It does present hundreds of helpful illustrations. It does present sensible, practical advice on the treatment of each type of cancer. Prognosis is given, often with a hopeful outlook.

MEDICAL NEWS



New Hearing Aids

Western Electrics two small and attractive all-in-one electronic hearing aids, were designed by Bell Telephone Laboratories to avoid compromises in meeting the individual requirements of hearing aid users. Without sacrificing acoustical performance in the conversational speech ranges, Model 65 (left) was designed with minimum size and weight and with sufficient power for the majority of users. Model 66 (right) has ample power for even severe cases and offers high fidelity acoustical performance.

Heart Disease Research

A new heart research center, a part of which is already in operation, will continue to develop at the Veterans Administration Mount Alto Hospital in Washington, D. C.

Ralph P. Robb, M. D., is a consultant to the unit which will have eight major functions: treatment; clinical research; cardiovascular roentgenography; cardiac catheterization and hemodynamics; electro-cardiography; pathology; statistical research and post-graduate teaching. Ultimately, departments for research in biochemistry and biophysics will be added.

It will also serve as a training center for VA doctors by providing post graduate study and resident training for certification by the American Board of Internal Medicine.

It further will provide consultation service in cardiovascular disease through treating difficult and selected cases and those cases requiring diagnostic procedures not elsewhere available.

The Hospital Program

The Hospital Survey and Construction Act, which became law in August 1946, has launched the most comprehensive program in the history of this country for the construction of hospitals and health facilities. To help communities realize the benefits of this legislation, the U. S. Public Health Serve has issued a series of five pamphlets.

The Hospital Survey and Construction Act is a summary of the law and regulations. *Why We Need More Hospitals* gives the story of hospital needs in this country. *The Hospital Act and Your Community* tells in simple terms what the program means to states and com-

(*Continued on page 15*)

Zemmer PHARMACEUTICALS

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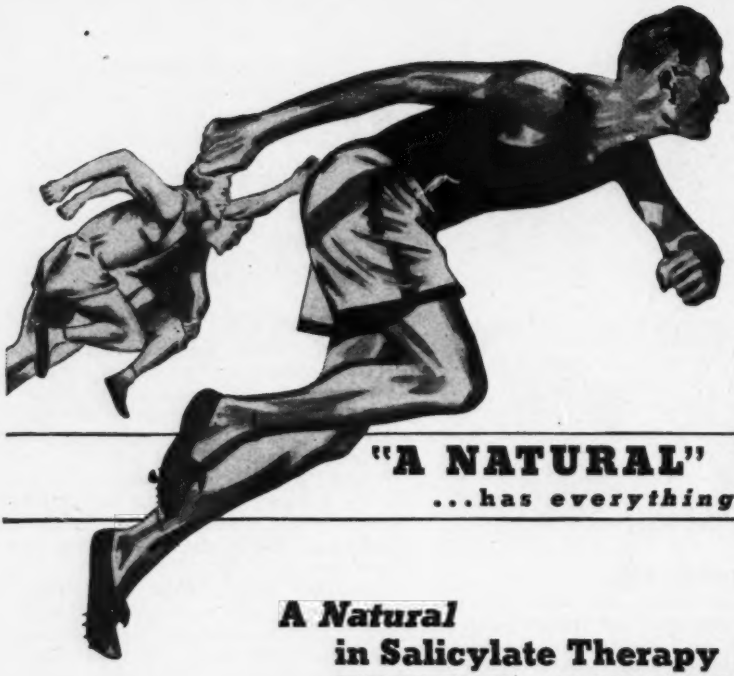
In the Treatment of Whooping-cough and Adult Irritating Bronchial Coughs

The pharmacologic action and the therapeutic effect of Auri-tussin, a solution of Gold Tribromide, in Whooping-cough is due to the antiseptic action of the Gold and the neuro-sedative action of the bromide. Supplied in ½-oz. dropper bottles. *Literature and prices on request.*



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Alysine Powder, containing approximately 0.6 Gm. (10 grs.) natural salicylates and 1.2 Gm. (20 grs.) alkaline salts per level teaspoonful, in 1-oz., 4-oz., and 1-lb. bottles.

In the symptomatic treatment of the common cold, influenza, la grippe, tonsillitis, rheumatic fever and arthritis, Elixir Alysine is the *natural* choice.

Containing *natural* salicylates prepared solely from oil of sweet birch, together with selected alkaline salts, Alysine provides fast, intensive salicylization with a minimum of gastric irritation or systemic acidotic tendency.

In a palatable, aromatized solution, Elixir Alysine is immediately assimilable for quick therapeutic response and readily adaptable to fractional dosages.

Used adjunctively with the sulfas, Alysine provides an alkaline (tolerance) factor, and at the same time helps to relieve muscular aches and pains.

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THE AURICLE SPEAKS

(*Continued from page 13*)

munities. *Hospital Quiz* is a series of questions and answers on hospital planning. *What is a Hospital System?* describes a coordinated hospital system, intended to extend the scope of hopsital care. Sample copies of these pamphlets are available free on request to the U. S. Public Health Service, Washington 25, D. C.

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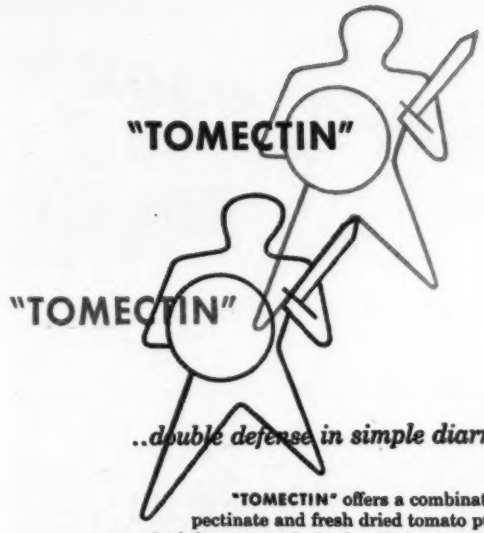

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[1] Block, L. H., Tarnowski, A., and Green, B. L.: Am. J. Digest. Dis. *6*:96 (Apr.) 1939
[2] Morrison, L. M.: Am. J. Digest. Dis. *13*:196 (June) 1946

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To only those who are bereft
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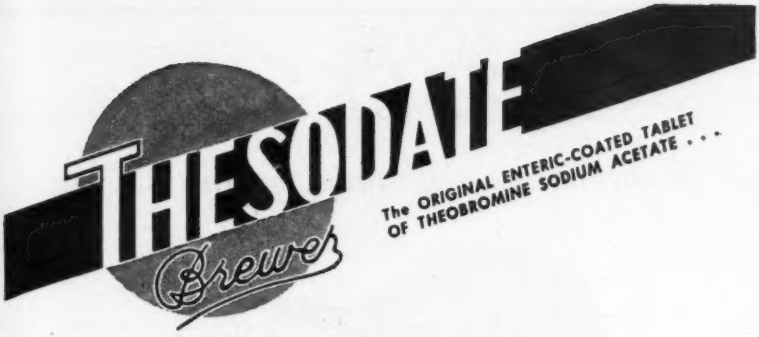

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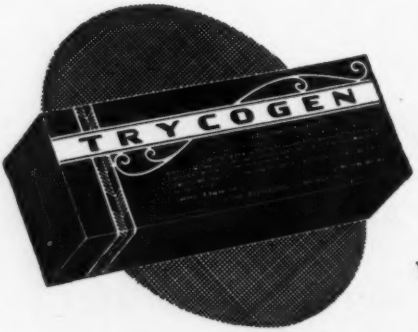

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**Woodhull, Robert B.: "Treatment of Trichomonas Vaginalis Vaginitis with Trycogen," Med. Rec. 155:474-477 (Oct. 1942).*

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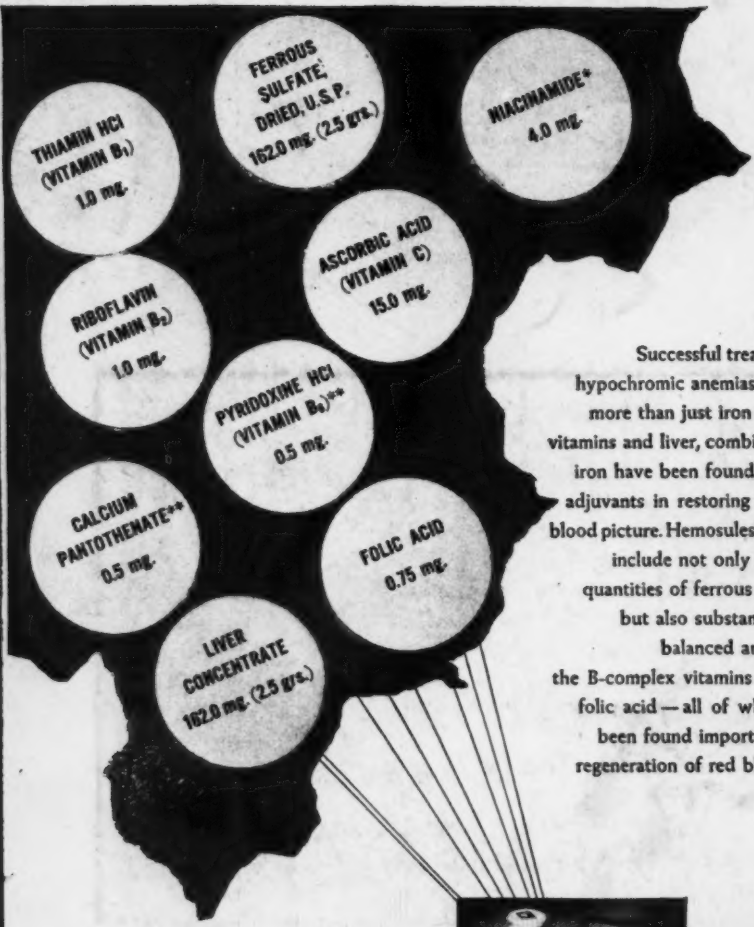

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